Efficacy of Prophylactic Ketamine in Preventing Postoperative Shivering

Profilaktik Ketamin Uygulamasının Postoperatif Titreme Üzerine Etkisi

Postoperatif Titreme ve Ketamin / Postoperative Shivering and Ketamine

Emine Arzu Köse[1], Mehtap Honca[2], Seda Banu Akıncı[3], Didem Dal[4], Ülkü Aypar[3]
[1]Department of Anesthesiology and Reanimation, Kirikkale University School of Medicine, Kirikkale,
[2]Department of Anesthesiology and Reanimation, Kecioren Teaching and Medical Research Hospital, Ankara,
[3]Department of Anesthesiology and Reanimation, Hacettepe University School of Medicine, Ankara,
[4]Department of Anesthesiology and Reanimation Marmara University School of Medicine, Istanbul, Turkey

Özet

Amaç: Ketamin ve meperidin postoperatif titreme tedavisinde etkili ajanlardır. Bu çalışmanın amacı, değişik ketamin dozlarının postoperatif titremeyi önleyici etkisinin plasebo ve meperidine ile karşılaştırılarak araştırılmasıdır. Gereç ve Yöntem: Bu randomize, çift-kör çalışmaya genel anestezi uygulanan ASA I ve II, 150 hasta dahil edilmiştir. Hastalar randomize olarak cerrahi işlemin bitiminden 20 dakika önce intravenöz yolla %0.9 serum fizyolojik (Grup S, n=30), meperidin 20 mg (Grup M, n=30), ketamin 0.1 mg/kg (Grup K1, n=30), ketamin 0.25 mg/kg (Grup K2, n=30) ve ketamin 0.5 mg/kg (Grup K5, n=30) verilecek gruplara ayrılmıştır. Anestezi indüksiyonunda 2 mg/kg propofol, 1 µg/kg fentanil ve 0.1 mg/kg veküronyum, idamesinde % 60 nitröz oksit - %40 oksijen karışımı içinde %2-3 sevofluran kullanılmıştır. Anestezi indüksiyonundan hemen sonra, indüksiyon sonrası 30. dakikada ve çalışmada kullanılan ilaçların verilmesinden önce timpanik ısı ölçümleri yapılmıştır. Postoperatif titreme 4 noktalı skala ile ve postoperatif ağrı vizüel ağrı skalası (VAS) ile 0-10 arasında bir değerle kaydedilmiştir. Bulgular: Derlenme odasına alındığında ve ameliyat sonrası 10. dakikalarda titreme gözlenen hastaların sayısı Grup M ve K5'de, Grup K1, K2 ve Grup S'ye göre istatistiksel olarak anlamlı olarak daha azdı ($p < 0.001$ ve $p= 0.001$). İlk analjezik ihtiyacı Grup M ve K5'de, Grup K1, K2 ve Grup S'ye göre dah uzun süre sonra ortaya çıktı ($p < 0.001$) . VAS bakımından gruplar arasında istatistiksel olarak farklılık gözlenmedi ($p > 0.05$). Sonuç: Proflaktik olarak verilen 0.5 mg/kg ketamin postoperatif titremenin önlenmesinde etkilidir; fakat 0.1 mg/kg ve 0.25 mg/kg dozlarda kullanıldığında proflaktik etkisi yoktur.

Anahtar Kelimeler

Ketamin; Meperidin; Postoperatif Titreme; Genel Anestezi

Abstract

Aim: Treatment with ketamine and meperidine is effective in postoperative shivering. The aim of this study was to investigate the minimum effective dose of ketamine in the prevention of postanaesthetic shivering compared to placebo and meperidine. Material and Method: This prospective randomized double-blind study involved 150 ASA I and II patients undergoing general anesthesia. Patients were randomly allocated to receive normal saline (Group S, n=30), meperidine 20 mg (Group M, n=30), ketamine 0.1 mg/kg (Group K1, n=30), ketamine 0.25 mg/kg (Group K2, n=30) and ketamine 0.5 mg/kg (Group K5, n=30) intravenously 20 minutes before completion of surgery. The anesthesia was induced with propofol 2 mg/kg, fentanyl 1 µg/kg and vecuronium 0.1 mg/kg. It was maintained with sevoflurane 2-3% and nitrous oxide 60% in oxygen. Tympanic temperature was measured immediately after induction of anesthesia, 30 minutes after induction and before administration of the study drug. Postoperative shivering was recorded using a four point scale and postoperative pain using a visual analogue scale (VAS) ranging between 0 and 10. Results: The number of patients shivering on arrival the recovery room and at 10 minutes after operation were significantly less in Groups M and K5 than in Groups K1, K2 and Group S ($p < 0.001$ and $p=0.001$). The time to first analgesic requirement in Groups M and K5 was longer than in the Groups K1, K2 and Group S ($P< 0.001$). There was no difference between the five groups regarding VAS pain scores ($p > 0.05$). Discussion: Prophylactic usage of ketamine 0.5 mg/kg was effective to prevent postanaesthetic shivering, but ketamine 0.1 mg/kg and 0.25 mg/kg had no prophylactic effect.

Keywords

Ketamine; Meperidine; Postoperative Shivering; General Anesthesia

DOI: 10.4328/JCAM.641 Received: 07.03.2011 Accepted: 18.03.2011 Printed: 01.04.2012 J Clin Anal Med 2012;3(2): 182-5
Corresponding Author: Emine Arzu Köse, Kirikkale University School of Medicine, Department of Anesthesiology and Reanimation, Kirikkale, Turkey.
T.: +903182252485 GSM: +905336802589 E-Mail: arzuhct@hotmail.com

Introduction

Postoperative shivering develops in 6.3%- 66 % of patients while recovering from general anesthesia [1]. This may be thermoregulatory shivering in response to core hypothermia or due to cytokines by the surgical procedure. The second type of shivering is non-thermoregulatory shivering and may occur in normothermic patients in response to certain anesthetics or postoperative pain [1,2]. It can trigger deleterious complications such as hypoxemia, raised oxygen consumption, lactic acidosis, increased intracerebral and intraocular pressure, raised carbon-dioxide production. Moreover, it may also induce pain secondary to muscular contractions at the site of operation and can lead interference with monitoring of ECG and blood pressure [1, 3, 4]. Several drugs are used for prophylaxis and therapy of postanesthetic shivering, including, meperidine, sufentanil, alfentanil, tramadol, ketanserin, uropidil, nefopam, doxapram, physostigmine, clonidine and nalbuphine [3-8]. Although its mechanism of action is not comletely understood, meperidine has been shown to be one of the most effective pharmacological agents [8, 9]. Ketamine, which is competitive N-methyl-D-aspartate (NMDA) receptor antagonist, has been shown to be effective in the prophylaxis of postoperative shivering in our previous study [10]. However, the ideal dose of ketamine in the prevention of shivering has not been determined. The aim of this study was to investigate minimum effective dose of ketamine in the prevention of postanesthetic shivering compared to placebo and meperidine.

Material and Method

Following approval of local ethics committee and written informed consent, we studied 150 patients of both genders aged 18-65 years. All patients were ASA physical status I or II and were undergoing general anesthesia for an anticipated duration of 60-180 minutes. Patients with Body Mass Index (BMI) > 30 kg/ m² and those with a history of convulsions, hypertension, multiple allergies, coronary artery disease or other cardiorespiratory or neuromuscular pathology were excluded. Procedures which might require adminisration of blood products and urological endoscopic operations were also excluded. All patients were informed about the visul analogue scale (VAS) before the operation. Patients were randomly allocated one of five groups:,

Group S received saline 0.9% as placebo (n=30);
Group M received meperidine 20 mg (n=30);
Group K 1 received ketamine 0.1 mg/kg (n=30);
Group K 2 received ketamine 0.25 mg/kg (n=30);
Group K 5 received ketamine 0.5 mg/kg (n=30).

Randomization was performed using closed envelopes.and all study drugs were diluted in a fixed volume of 2 ml and presented as coded syringes by an anesthetist who was not involved in the management of patients for this prospective, randomised, double-blind, controlled study. Demographic data, heart rate, non-invazive blood pressure and oxygen saturation were recorded before and during surgery. Tympanic temperature was measured using a First Temp Genius Model 3000 A aural canal thermometer (Sherwood Medical Company, St. Louis) before anesthesia, immediatealy after induction of anesthesia, 30 minutes after induction and before administration of the study drug. We planned to exclude patients with tympanic temperature < 35 º C, and to actively warm those with tympanic temperatures between 35-36 ºC. Anesthesia was induced using propofol 2 mg/kg and fentanyl 1 µg/kg, and vecuronium 0.1 mg/kg was given to facilitate orotracheal intubation. Anesthesia was maintained with nitrous oxide 60 % in oxygen and sevoflurane 2-3 %. Muscle relaxation was supplemented as required using boluses of vecuronium 0.03-0.05 mg/kg. Approximately 20 minutes before completion of surgery the study drug was administered intravenously regarding to study groups. Residual neuromuscular blockade was reversed using neostigmine 0.03 mg/kg and atropine 0.01 mg/kg and when the patient's respiratory effort was adequate the trachea was extubated. The type and duration of anesthesia and surgery were recorded.

The postoperative evaluation of patients and their shivering score was assessed by an anesthesiologist in the recovery room, who was unaware of patient grouping. All patients were monitored, received oxygen via a facemask and were covered with a cotton blanket. Heart rate, non-invasive blood pressure, oxygen saturation, tympanic temperature and shivering score were measured and recorded on admission to the recovery room (T0), and 10 minutes (T10), 20 minutes (T20), 30 minutes (T30) thereafter. The shivering was graded using a four-point scale (Table 1), and the pain was assesssed using a 0-10 cm visual analogue scale (VAS), where 0=no pain and 10=worst pain imaginable. The pain assessments were made on admission to the recovery room (T0), at the first (T1) and second (T2) hours in the recovery room. Any possible side-effects of study drugs (i.e. nausea, vomiting, hypotension, tachycardia, hypertenion or hallucinations) were recorded. Patients with nausea or vomiting were treated with metoclopramid 10 mg i.v. Postoperative pain was treated with methamizole 1000 mg i.v. during the first 30 minutes and with meperidine 20 mg i.v. after 30 minutes for VAS > 3. The shivering was treated with meperidine 20 mg i.v. if the shivering grade was ≥ 2. The administration times and amounts of drugs given in the postoperative 2 hours were recorded.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) Windows version 11.5. Mean differences between the five groups regarding age, weight, height, duration of anesthesia, duration of operation, haemodynamic parameters, tympanic temperatures and the first analgesic requirement time were tested using analysis of variance (ANOVA). Pain scores were compared using the Kruskal-Wallis test. The X^2 test was used to analyse the difference between gender, ASA class, type of surgery, the number of shivering patients, those who required analgesics and who had vomiting- nausea, nystagmus, feeling like walking in the space. Post hoc comparisons were performed using the Benforroni correction of the significance level. We expected an incidence of shivering in the placebo group of at least 50 and a reduction of the incidence to about 15% with an effective medication. Consequently, to detect a reduction in incidence from 50% to 15% with an α-error of 0.05 and a β-error of 0.2, a minimum of 27 patients per group was required. All values are expressed as mean (SD) or as median (range). P values < 0.05 were considered significant.

Table 1. Classification of shivering

Grade	Clinical signs
0	No shivering
1	Mild fasciculations of face or neck
2	Visible tremor involving more than one muscle group
3	Gross muscular activitiy involving entire body

Results

All groups were similar with regard to age, weight, height, gender, duration of anesthesia, duration of operation, type of surgery and ASA classification (Table 2). The haemodynamic parameters and tympanic temperatures were also comparable in five groups. Because of the tympanic temperatures of the patients were > 36 ºC, active warming was not required.

The number of patients with postoperative shivering on arrival in the recovery room and at 10 minutes after arrival were significantly less in Group M and Group K5 than Group S, Group K1, Group K2 (Table 3). There was no difference between Group M and Group K5 ($p > 0.05$) and there were no significant differences between Group S, K1 and K2 ($p > 0.05$). The number of patients required to treat with meperidine 20 mg i. v. because of shiverig at grade ≥ 2 were 14,10 and 5 in Group S, K1 and K2 respectively. In group M and K5, none of the patients shivered. At 20 minutes and 30 minutes after operation, there were no significant differences between five groups (Table 3). None of the patients required a second dose of meperidine for a shivering grade ≥ 2 within the 30 minutes period.

The first analgesic requirement time was significantly longer in Group M (27.6 ± 11.7 min) and Group K5 (27.3 ± 11.5 min) than that in Group S (17.2 ± 7.4 min), Group K1 (17.7 ± 5.9 min), Group K2 (16.9 ± 6.0 min) ($P < 0.001$). During thirty minutes after operation, 21 patients in group S, 15 in Group M, 20 in Group K5, 19 in Group K2 and 21 in Group K1 were treated with i. v. methamizole ($P > 0.05$). After the 30 minutes period, within the first postoperative hour, 20 patients in Group S, 13 in Group M, 12 in Group K5, 15 in Group K2 and 17 in Group K1 had VAS scores > 3 and they were treated with i.v. meperidine ($p > 0.05$). There was no difference between the five groups regarding VAS scores (Table 4). Five patients in Group K5, eight each in Groups M and K2, nine each in Groups S and K1 had VAS scores > 3 and they were treated with i.v. meperidine in the second postoperative hour ($p > 0.05$).

Six patients in Group S, one in Group K5 and two in K2, four in Group K1, seven in Group M had nausea and vomiting ($p > 0.05$). Respiratory depression or episodes of oxygen desaturation, hallucinations, tachycardia, hypotension, hypertension, nystagmus and feeling like walking in the space, were not observed in any of the patients during the study.

Discussion

Postanesthetic shivering is a common and undesirable complication of general anesthesia. It is defined as an involuntary movement of one or several muscle groups and occurs in up to 66% of patients recovering from general anaesthesia [1]. In this study, 16 of 30 patients (53.3%) in the control group shivered postoperatively. This incidence is in accordance with various other clinical investigations [3, 5, 6].

All anesthetic agents impair thermoregulatory responses by lowering the shivering threshold and decreasing vasoconstruction resulting in a higher tolerance to core hypothermia without initiation of thermoregulatory responses. During recovery from anesthesia thermoregulatory centers are no longer inhibited, shivering is triggered and becomes apparent [11]. Postanesthetic shivering can be accompanied by a drop in core temperature, but its correlation with hypotermia is poor and can be observed during normothermia as well [1, 2, 11]. In this study there were no significant differences in tympanic temperature among the five groups. The tympanic temperatures of the patients were > 36 ºC and there was no need for active warming.

Table 2. Patient characteristics of the five groups

	Group S (n=30)	Group M (n=30)	Group K1 (n=30)	Group K2 (n=30)	Group K5 (n=30)
Age (yr)	44.5 ± 9.2	44.7 ± 12.3	41.9 ± 14.0	37.4 ± 10.8	44.1 ± 10.1
Female/male (n)	27/3	24/6	19/11	23/7	20/10
Weight (kg)	67.9 ± 11.7	72.2 ± 9.3	71.2 ± 10.6	68.9 ± 14.6	74.1± 7.2
Height (cm)	162.8 ± 6.7	164.8 ±8.0	165.9 ± 6.9	164.6 ± 8.2	168.1 ± 10.7
ASA I/II (n)	22/8	26/4	29/1	27/3	25/5
Duration of anesthesia (min)	103.0 ±32.6	105.3 ± 32.0	98.5 ± 30.1	98.8 ± 28.9	108.3 ± 32.9
Duration of operation (min)	93.5 ± 32.5	96.5 ± 32.5	90.5 ± 29.0	91.3 ± 27.8	98.3 ± 32.9
Type of surgery					
-Laparoscopic cholecystectomy (n)	9	9	12	11	10
-Thyroidectomy (n)	5	4	3	1	3
-Parathyroidectomy (n)	1	1	0	2	1
-Umblical hernia (n)	4	4	4	2	2
-İnguinal hernia (n)	11	11	11	13	13
-Mastectomy (n)	0	1	0	1	1

Data are presented as mean ± SD or absolute numbers.

Several drugs are used to prevent postanesthetic shivering [1, 3-10]. Meperidine has been shown to be one of the most effective drugs [8, 9]. Although its mechanism of action is not completely understood, it probably acts directly on the thermoregulatory centre [7] or via opioid receptors [12]. In our study, none of the patients shivered after prophylactic meperidine. The opioid receptor agonist meperidine has a high affinity for μ receptors, and a moderate affinity for σ and δ receptors. Meperidine is more effective in treating shivering than are equianalgesic doses of relatively pure μ receptor agonists, such as morphine and fentanyl [13]. These data indicate thatσreceptor stimulation may contribute to meperidine's anti-shivering effect. Additional support for this theory comes from observation that the anti-shivering effect of meperidine was inhibited by high-dose naloxone, which blocks μ andσreceptors, but not by low-dose

Table 3. Number of patients with different grades of shivering in the five treatment groups

	Grade 0/1/2/3					P-value
	Group S	**Group M**	**Group K1**	**Group K2**	**Group K5**	
T0	14/2/5/9	30/0/0/0*	18/2/4/6	20/5/2/3	30/0/0/0**	< 0.001
T10	20/0/5/5	30/0/0/0*	20/0/5/5	19/2/5/4	30/0/0/0**	0.001
T20	25/5/0/0	30/0/0/0	27/3/0/0	26/4/0/0	28/0/2/0	0.212
T30	28/2/0/0	30/0/0/0	28/2/0/0	28/2/0/0	29/1/0/0	0.663

T0, arrival in the recovery room; T10, 10 min after arrival; T20, 20 min after arrival; T30, 30 min after arrival. *p< 0.05 between Group M and Group S, Group K1, Group K2; **p < 0.05 between Group K5 and Group S, Group K1, Group K2.

Table 4. Pain scores

	Group S	Group M	Group K1	Group K2	Group K5	P value
VAS0	6 (2-8)	6 (2-8)	6 (2-8)	6 (2-8)	6 (2-8)	0.470
VAS1	5 (2-6)	4 (1-6.4)	5 (2.1-6)	4 (1.5-6.4)	6 (2-6)	0.284
VAS2	5 (1.5-6)	5 (1.5-6)	5 (1.5-6)	5 (2-6)	5 (1.5-6)	0.197

Pain scores using Visual Analogue Scale (VAS) expressed as median (5th-95th percentile) in the five groups. VAS0, on arrival in the recovery room; VAS1, at first postoperative hour; VAS2, at second postoperative hour.

naloxone which blocks μ receptors only [14]. Nausea and vomiting are well known and common side-effects of meperidine. Another disadvantage of meperidine is that it can cause respiratory depression in the presence of previously administered opioids or anesthetics.

Ketamine, a noncompetitive NMDA receptor antagonist, has been shown to inhibit postoperative shivering [10, 15-17]. Secondary to an inhibition of norepinephrine uptake into postganglionic sympathetic nerve endings it has been shown that ketamine has the ability to decrease core-to-peripheral redistribution of the heat [18]. Moreover, it is likely that NMDA receptor antagonists also modulate thermoregulation at multipl levels [12, 19]. In addition to being a competitive NMDA receptor antagonist, ketamine has several other pharmacological properties; these include being aσopioid agonist, blocking amine uptake in the descending inhibitory monoaminergic pain pathways, having a local anesthetic action and interacting with muscarinic receptors. Therefore it probably controls shivering by non-shivering thermogenesis either by action on the hypothalamus or by the β-adrenergic effect of norepinephrin [12, 17]. In our previous study, we found that prophylactic administration of ketamine 0.5 mg/kg intravenously was effective in preventing postoperative shivering [10]. In the present dose-ranging study, we investigated the minimum effective dose of ketamine in preventing postoperative shivering and showed that ketamine 0.5 mg/kg was effective to prevent postanesthetic shivering, but ketamine 0.1 mg/kg and 0.25 mg/kg had no prophylactic effect. In this study, two patients still had grade ≥ 2 shivering after ketamine 0.5 mg/kg prophylaxis and were treated with i.v. meperidine. This condition can be explained with meperidine and ketamine have different mechanisms of action. We found no difference between the efficacy of ketamine 0.5 mg/kg and meperidine 20 mg similar to our previus study [10]. We did not choose to compare 0.5 mg/kg ketamine with higher doses of ketamine because of it was shown that 0.5 mg/kg and 0.75 mg/kg ketamine doses have similar effect for

the treatment of postoperative shivering and the side-effects were increased with higher doses in a previous study [15].

Sharma and colleagues, reported that ketamine was usefull in the treatment of postanesthetic shivering but two of 30 patients inolving the study developed hallucinations and four of them developed delirium [17]. In another study, it was reported that none of 30 patients had hallusinations or delirium when ketamine was given approximately 20 minutes before completion of surgery under general anesthesia [10]. Although none of our patients had hallucinations and delirium, this side-effects of ketamine should always be kept in mind.

In the postoperative period, nystagmus and feeling like walking in the space were not observed in any patients. This lack of side-effects was similar with the study reported by Dal and colleagues [10] which they used ketamine 0.5 mg/kg approximately 20 minutes before completion of surgery under general anesthesia. and may be explained by the short duration of action of ketamine and/or because this side effects were masked by the effect of general anesthesia.

In the postoperative period, the time to first analgesic requirement in the meperidine group and the ketamine 0.5 mg/kg group was longer than that in the control group and ketamine 0.25 mg/kg and 0.1 mg/kg groups. All patients needed to analgesia with methamizole or pethidine in the first 2 hour after operation and this can be explained by the short duration of action of meperidine 20 mg and ketamine 0.5 mg/kg. Although there are not enough data to draw firm conclusions about methamizole, both methamizole and meperidine supress postanesthetic shiverig [20, 21]. Methamizole given for the pain relief in the first 30 minutes might have augmented the antishivering effects of ketamine or meperidine.

The most important disadvantages of meperidine are nausea-vomiting and its interaction with previously administered opioids or anesthetics, leading to respiratory depression. Although this study did not have sufficient power to show any difference between the two drugs, ketamine may have at least theorical advantages over meperidine regarding respiratory depression, nausea and vomiting. In conclusion, ketamine can be an alternative prophylaxis against postoperative shivering in patients with bradycardia, hypotension, respiratory depression, nausea, vomiting and allergic reactions to meperidine.

References

1. Alfonsi P. Postanaesthetic shivering: Epidemiology, pathophysiology, and approaches to prevention and management. Drugs 2001; 61(5): 2193-205.
2. Horn EP, Sesler DI, Standl T, Schroeder F, Bartz HJ, Beyer JC, Schulte am Esch J. Non-thermoregulatory shivering in patients recovering from isoflurane or desflurne anesthesia. Anesthesiology 1998; 89 (4) : 878-86.
3. Piper SN, Suttner SW, Schmidt CC, Maleck WH, Kumle B, Boldt J. Nefopam and clonidine in prevention of postanaesthetic shivering. Anaesthesia 1999; 54 (7) : 695-99.
4. Piper SN, Fent MT, Röhm KD, Maleck WH, Suttner SW, Boldt J. Uropidil does not prevent postanesthetic shivering: a dose- ranging study. Can J Anesth 2001; 48 (8) : 742-7.
5. Singh P, Dimitriou V, Mahajan RP, Crossley AWA. Double- blind comparison between doxapram and pethidine in treatment of postanaesthetic shivering. Br J Anaesth 1993; 71 (5) : 685-8.
6. Mathews S, Al Mulla A, Varghese PK, Radim K, Mumtaz S. Postanaesthetic shivering- a new look at tramadol. Anaesthesia 2002; 57 (4) : 394-8.
7. Vanderstappen I, Vandemeerch E, Vanacker B, Mattheussen M, Herijgers P, Van Aken H. The effect of prophylactic clonidine on postoperative shiverig: a large prospective double-blind study. Anaesthesia 1996; 51 (4) : 351-5.
8. Wrench IJ, Cavill G, Ward JEH, Crossley AWA. Comparison between alfentanil, pethidine and placebo in the treatment of post-anaesthetic shivering. Br J Anaesth 1997; 79 (4) : 541-2.
9. Terasako K, Yamamoto M. Comparison between pentazosine, pethidine and placebo in the treatment of post-anaesthetic shivering. Acta Anaesthesiol Scand 2000; 44 (3) : 311-2.
10. Dal D, Kose A, Honca M, Akinci SB, Basgul E, Aypar U. Efficacy of prophylactic ketamine in preventing postoperative shivering. Br J Anaesth 2005; 95 (5) : 189-92.
11. Buggy DJ, Crossley AWA. Thermoregulation, mild perioperative hypothermia and postoperative shivering. Br J Anaesth 2000; 84 (5) : 615-28.
12. De Witte J, Sesler DI. Perioperative shivering: physiology and pharmacology. Anesthesiology 2002; 96 (2) : 467-84.
13. Pauca AL, Savage RT, Simpson S, Roy RC. Effect of pethidine, fentanyl and morphine on postoperative shivering in man. Acta Anaesthesiol Scand 1984; 28 (2) : 138-43.
14. Kurz M, Belani KG, Sessler DI, Kurz A, Larson MD, Schroeder M, Blanchard D. Naloxone, meperidine, and shivering. Anesthesiology 1993; 79 (6) : 1193-201.
15. Kose EA, Dal D, Akinci SB, Saricaoglu F, Aypar U. The efficacy of ketamine for the treatment of postoperative shivering. Anesth Analg 2008; 106 (1) : 120-2.
16. Piper SN, Beschmann R, Mengistu A, Maleck WH, Boldt J, Röhm KD. Postoperative analgosedation with S (+)-ketamine decreases the incidences of postanesthetic shivering and nausea and vomiting after cardiac surgery. Med Sci Monit 2008; 14 (12): 159-65.
17. Sharma DR,Thakur JR. Ketamine and shivering. Anaesthesia 1990; 45 (3) : 252-3.
18. Ikeda T, Kazama T, Sesler DI, Toriyama S, Niwa K, Shimada C, Sato S. Induction of anesthesia with ketamine reduces the magnitude of redistribution hypothermia. Anesth Analg 2001; 93 (4) : 934-8.
19. Canini F, Bourdon I, Bittel J. Effect of ambient temperatures ranging from cold to heat on thermoregulation in couscious MK801-treated rats. Can J Physiol Pharmacol 2003; 81 (10) : 959-65.
20. Monso A, Riudeubas J, Barbal F, Laporte JR, Arnau JM. A randomized, double-blind, placebo-controlled trial comparing to methamizole to treatment of post-anaesthetic shivering. Br J Clin Pharmacol 1996; 42 (3) : 307-11.
21. Kranke P, Eberhart LH, Roewe N, Tramer MR. Pharmacological treatment of postoperative shivering: A quantative systematic review of randomized controlled trials. Anesth Analg 2002; 94 (2) : 453-60.